DETAILED ACTION

Status of Claims

Response and Declaration under 37 CFR 1.132 filed 11/03/2009 are acknowledged.

There are no changes in claim status.

Claims 1-15 are pending. Claims 13-15 remain withdrawn from further consideration.

This application contains claims 13-15 drawn to an invention nonelected with traverse in the reply filed on 03/16/2009. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Applicant's arguments have been fully considered and were deemed to be persuasive-in-part. Rejections not reiterated from previous Office actions are hereby withdrawn. The following rejections are reiterated. They constitute the complete set presently being applied to the instant application.

Abstract

The abstract of the disclosure is objected to because an abstract on a separate sheet is required . Correction is required.

It is noted that applicant submitted "Amendment to Specification" on 11/03/2009, with indication of submission of an Abstract. However, no Substitute

Abstract, attached as suggested by statement on p. 2 of the response, has been received.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Väänänen et al (European Journal of Gastroenterology & Hepatology, 2003, 15(8), 885-891) or Suovaniemi (US 2004003837; now US Patent 7,358,062), in view of García-Fernández (Nephron 2002;92:97-104) and Ashton et al. (US 6,950,544).

The instant claims are drawn to method for assessing or predicting the state of the gastric mucosa in a subject by determining the probability for the gastric mucosa belonging to at least one gastric mucosa class, the method comprising

a) measuring, from a sample of said subject,

- the pepsinogen I (PGI) and
- gastrin-17 (G-17) analyte concentrations, as well as
- determining the presence or concentration of a marker for Helicobacter pylori

b) entering the data in a data processing system to determine the probability for the gastric mucosa belonging to the at least one gastric mucosa class based on

- the data entered, as well as
- on predefined clinical data in the database,

the information so generated by the data processing system being indicative of the state of the gastric mucosa in said subject

Väänänen et al teach measuring in a subject

- serum levels of gastrin-17 (S-G-17),
- pepsinogen I (S-PGI), and
- assaying *Helicobacter pylori* antibodies

Gastrin and pepsinogen levels were compared with clinical history of patients. S-G-17_{prand} (and S-G-17_{fast}) and S-PGI levels decreased with increasing grade of atrophy of the antrum or corpus, respectively. S-G-17_{prand} levels were significantly lower in patients with advanced (moderate or severe) atrophic antral *H. pylori* gastritis than in those with non-atrophic *H. pylori* gastritis. All patients with a resected antrum demonstrated S-G-17_{prand} levels that were almost undetectable.

Similarly, comparing *H. pylori*-positive antibody assay results with clinical history demonstrated correlation of *H. pylori* assay results with atrophic antral gastritis Similarly, S-PGI levels were significantly lower in patients with advanced corpus atrophy than in those without.

The sensitivity and specificity of the blood test panel in delineation of patients with advanced atrophic gastritis (either in the antrum or the corpus, or both) were 83% and

95%, respectively. The predictive values of the positive and negative test results were 75% and 97%, respectively.

Thus, the reference teaches measuring the said markers and determining the probability for the gastric mucosa belonging to advanced atrophic gastritis, either in the antrum or the corpus or both, based on the results of the measurements combined with clinical data .

Suovaniemi (US 20040038376; now US Patent 7,358,062) teaches a method for assessing the condition of the gastric mucosa, especially for diagnosing mucosal gastric changes, such as atrophic gastritis, in a subject, by assaying the analytes

- pepsinogen I (PGI),
- gastrin, and
- a marker for Helicobacter pylori infection,

the method comprising measuring from a sample of said subject the pepsinogen I and gastrin concentration, and, in addition, determining the concentration or presence of a marker for Helicobacter pylori, entering the data so obtained for said analytes in a data processing means comprising an operating system, means for transceiving and processing data, said data processing means being adapted to perform the steps of comparing a measured concentration value for an analyte to a predetermined cut-off value for said analyte, to obtain a combination of comparison results which is specific for the subject tested, and generating information in response to the said combination of comparison results.

Further, with respect to claim 10, Suovaniemi et al teach further measuring pepsinogen II (PGII), forming a PGI/PGII ratio and entering said PGI/PGII ratio into said data processing system (see claim 5).

The references do not teach determining probability for the gastric mucosa to belong to atrophic gastritis tissue.

However, high level of predictive values correlating levels of the markers discussed above with the presence or absence of atrophic gastritis tissue make it obvious that measuring the amounts/presence of these markers can be used to determine probability that a tissue belongs to a particular condition of interest.

Regression analysis of clinical data is routinely used to determine probabilities of events or occurrences of interest. As an example, **García-Fernández** teaches using prediction model based on applying of univariate and multivariate logistic regressions of clinical data comprising levels of PAI-1 antigen, t-PA antigen, and prothrombin fragment to determine probability of death outcome. See Abstract and p. 99, left column.

Furthermore, it is known that when a plurality of parameters (markers) are known, probability of a tissue to belong to a certain type can be determined using "probability maps". See US 6950544 (**Ashton** et al) , for example, wherein the probability map represents a probability that each of the plurality of structures is found in any given image element. Although US 6950544 is directed to use of image information – as opposed to marker presence in the instant invention – it would be obvious to apply the same approach to gastrin and pepsinogen and H. pilori data. Consequently, it would be obvious to use the system for automated probability determination comprising operation system, database and suitably programmed processor, such as system

taught in US 6950544 (see claim 46), to determine probability of predicting a state of gastric mucosa using markers discussed in Väänänen et al.

Further, with regard to using a "data processing system", as instructed by MPEP, chapter 2106 II, merely using a computer to automate a known process does not by itself impart nonobviousness to the invention. The use of particular mathematical or computerized means would have accomplished the same result would be an obvious mathematical and/or computational way of determining and presentation of results.

With respect to dependent claims 2-9,11,12 if there are any differences between Applicant's claimed method and that of the prior art, the differences would be appear minor in nature. The nature of the problem to be solved – generating and using predictive clinical data - would lead inventors to look at references relating to possible factors known to determine selection of appropriate markers, data acquisition, analysis, presentation as well as future use of the predictive model. One of ordinary skill in the art would have been motivated to combine all known factors with no change in their respective functions, and the combination would have yielded nothing more than predictable results.

Response to arguments

Applicant argues that as demonstrated in the Declaration Dr. Sarna, one of skill in the art would not have found the present invention obvious because the present

invention applies the "Path model",. Examiner disagrees. the instant claims do not address application of a “Path model, addressed in applicant’s response as

a multinomial regression which results in probabilities of the certainty of the classification of the status of the gastric mucosa, and diagnosis of the subject

Rather, the claims are directed to method comprising the steps of obtaining data and entering them in a data processing system to determine probabilities of belonging to a particular gastric mucosa class. The rejection of record addresses not the disclosed but claimed subject matter.

Further, applicant argues that the secondary references of Ashton and Garcia-Fernfindez apply an algorithm for a different disease. Said references are cited merely to demonstrate that, in general, regression analysis of clinical data is routinely used to determine probabilities of events or occurrences of interest (Garcia-Fernfindez) and that “probability maps” are being used to determine probability of a tissue to belong to a certain type (Ashton). Applying known approaches without changing their known mode of operation to a particular situation of describing gastric mucosa is considered obvious to one skilled in the art. Further, applicant argues that the references use different statistic analysis. Majority of the claims are not directed to any particular statistic analysis; as for claim 5, García-Fernández teaches using prediction model based on applying of univariate and multivariate logistic regressions of clinical data.

Consequently, the Declaration under 37 CFR 1.132 filed 11/03/2009 is insufficient to overcome the art rejection of record for the above reasons.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of Suovaniemi et al (U.S. Patent No. 7,358,062) in view of García-Fernándes (Nephron 2002;92:97-104) and Ashton et al. (US 6,950,544).

US Patent 7,358,062 teaches a method for assessing the condition of the gastric mucosa, especially for diagnosing mucosal gas tric changes, such as atrophic gastritis, in a subject, by assaying the analytes pepsinogen I (PGI), gastrin and a marker for Helicobacter pylori infection, the method comprising measuring from a sample of said subject the pepsinogen I and gastrin concentration, and, in addition, determining the concentration or presence of a marker for Helicobacter pylori, entering the data so obtained for said analytes in a data processing means comprising an operating system, means for transceiving and processing data, said data processing means being adapted to perform the steps of comparing a measured concentration value for an analyte to a predetermined cut-off value for said analyte, to obtain a combination of comparison results which is specific for the subject tested, and generating information in response to the said combination of comparison results.

Further, with respect to claim 10, Suovaniemi et al teach further measuring pepsinogen II (PGII), forming a PGI/PGII ratio and entering said PGI/PGII ratio into said data processing system (see claim 5).

US Patent 7,358,062 does not teach determining probability for the gastric mucosa to belong to atrophic gastritis tissue.

However, high level of predictive values correlating levels of the markers discussed above with the presence or absence of atrophic gastritis tissue make it obvious that measuring the amounts/presence of these markers can be used to determine probability that a tissue belongs to a particular condition of interest.

Regression analysis of clinical data is routinely used to determine probabilities of events or occurrences of interest. As an example, García-Fernánde teaches using

prediction model based on applying of univariate and multivariate logistic regressions of clinical data comprising levels of PAI-1 antigen, t-PA antigen, and prothrombin fragment to determine probability of death outcome.

Furthermore, it is known that when a plurality of parameters (markers) are known, probability of a tissue to belong to a certain type can be determined using "probability maps". See US 6950544 (Ashton et al) , for example, wherein the probability map represents a probability that each of the plurality of structures is found in any given image element. Although US 6950544 is directed to use of image information – as opposed to marker presence in the instant invention – it would be obvious to apply the same approach to gastrin and pepsinogen and H. pilori data. Consequently, it would be obvious to use the system for automated probability determination comprising operation system, database and suitably programmed processor, such as system taught in US 6950544 (see claim 46), to determine probability of predicting a state of gastric mucosa using markers discussed in Väänänen et al.

Response to arguments

Applicant correctly points out that it is unclear which claims are subject of the rejection. Due to inadvertent error, the claim numbers were indicated incorrectly, and are corrected now.

Applicant further argues that claims 1-12 are not unpatentable over claims of U.S. Patent No. 7,358,062 for the reasons stated with regard to the rejection under 35 U.S.C. 103(a). As the latter rejection is maintained for the reasons set forth above, the double-patenting rejection is maintained.

Prior art made of record

The prior art made of record which had been considered pertinent to applicant's disclosure is reiterated herein.

WO 96/15456 a method for determining detecting atrophy of the corpus or antrum area of the stomach, or atrophy of the mucosa of the stomach by measuring concentration of the analytes pepsinogen I, and gastrin-17 from a serum sample of a subject; the said tests may be combined with a test for Helicobacter pylori antibodies. The determined concentration values are then compared to a cut-off value and a reference value for each analyte. A serum pepsinogen I concentration below the cut-off value for pepsinogen I in combination with a gastrin-17 concentration value above the upper reference limit indicates severe atrophy of the corpus area of the stomach. A serum gastrin-17 level below the cut-off value for gastrin-17 in combination with a pepsinogen I value above the cut-off value for pepsinogen I on the other hand indicates atrophy of the antrum area of the stomach. In case the serum pepsinogen I is below the cut-off value for pepsinogen I, and the gastrin-17 level is at the lower limit of its reference value, this is an indication of severe atrophy in the whole stomach, i.e. of atrophic pangastritis.

Valle et al teach a method of assessing the condition of the gastric mucosa through measuring pepsinogen, a Helicobacter pylori marker and gastrin in a subjects' sample and utilizes a computer for data analysis,

Harkonen (US Pat. 6,696,262) and Sipponen (Scandinavian journal of gastroenterology, (2002 Jul) Vol.37, No. 7, pp. 785-791) show measurement of PGI, Gastrin-17 and a Helicobacter marker

Schlemper et al (1995) is cited to show the measurement of gastrin, pepsinogen I, pepsinogen II and PGI/PGII (A/C) ratio as a measurement of changes in the mucosa (see Figure 1, page 199)

Conclusion.

No claims are allowed

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Borin/
Primary Examiner, Art Unit 1631